



MS AF
REPLY UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1654
PATENT
4867-0101PUS1

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: WANG, Chau-Jong Conf.: 9845
Appl. No.: 09/989,490 Group: 1654
Filed: November 21, 2001 Examiner: M. V. Meller
For: METHOD TO COUNTER OXIDATION OF LDL,
DECREASE TRIGLYCERIDE OR CHOLESTEROL
AND INHIBIT ATHEROSCLEROSIS USING
HIBISCUS SABDARIFFA EXTRACT

REPLY UNDER 37 C.F.R. § 1.116

MS AF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

May 28, 2004

Sir:

In response to the Office Action issued on November 28, 2004,
the due date having been extended for three (3) months to May 28,
2004, the following amendments and remarks are respectfully
submitted.

This reply includes Amendments to the Claims and Remarks.

AMENDMENTS TO THE CLAIMS

1. (currently amended) A method of treating artherosclerosis by decreasing ~~inhibiting~~ oxidation of low density lipoproteins which comprises administering an effective amount of a *Hibiscus sabdariffa* water extract to a patient in need thereof; wherein oxidation of low density lipoproteins is ~~inhibited~~ decreased by the *Hibiscus sabdariffa* water extract.

2-4. (cancelled)

5. (currently amended) The method of claim 1, further comprising combining the said *Hibiscus sabdariffa* water extract with a pharmaceutically acceptable carrier.

6. (currently amended) The method of claim 5 wherein the amount of the said *Hibiscus sabdariffa* water extract is administered in a pharmaceutical unit dosage form which is adapted for oral administration.

7. (original) The method of claim 6 wherein the unit dosage form is a tablet or a capsule

8-14. (cancelled)

REMARKS

Claims 1, 5-7 and 14 are pending in this application.

Statement regarding interview

Applicants would like to thank Examiner Meller for his time and consideration with the Interview of May 25, 2004. During the interview Applicants discussed both the rejection of the claims for lack of enablement and the rejections over the prior art.

Regarding the prior art, Applicants noted that there is no disclosure in any of the references of treating arteriosclerosis by decreasing/inhibiting the oxidation of LDL with an extract of *Hibiscus sabdariffa*. As indicated on the Interview Summary Record, the Examiner indicated that if the claims were limited to methods of treating arteriosclerosis by decreasing/inhibiting the oxidation of LDL with the recited extract, both the enablement and prior art rejections should be overcome.

Rejections under 35 U.S.C. §112, 1st paragraph

The Examiner has rejected the claims under 35 U.S.C. §112, 1st paragraph for lack of enablement with regard to the recitation of "inhibiting" oxidation of LDL with the assertion that "inhibiting" would require 100% inhibition. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The online dictionary of YourDictionary.com defines "inhibit" when used in biology as meaning "To decrease, limit, or block the action or function of." See the attached printout of Exhibit A. In addition, in reporting results of a response that is blocked to any extent one states that the response is "inhibited." It is not required that a response be blocked 100% to be "inhibited." As such, claim 1 does not require that the oxidation be 100%. However, in an effort to facilitate the prosecution of the application, claim 1 has been amended to recite, "A method of decreasing oxidation...." In addition, claim 1 has been amended as suggested by the Examiner to be limited to a method of treating atherosclerosis with a water extract of *Hibiscus sabdariffa*. Withdrawal of the rejection is therefore respectfully requested.

Rejections under 35 U.S.C. §102

Claim 14 has been rejected under 35 U.S.C. §102 as being anticipated by Brink, CN 1156552, JP56029522A, FR 2454277A, JP 2000095663, JP 2000239164, JP 09295928, JP2000154134, Ibnsaud et al. and Clarke et al. Claim 14 has been cancelled; however inasmuch as the rejections may apply to amended claim 1, Applicants traverse these rejections and withdrawal thereof is respectfully requested. Applicants address the distinguishing features of the invention from each the references below. In addition, attached

hereto is Table 1 which succinctly summarizes the teachings of the prior art relied on by the Examiner. It can be seen from the table that none of the references teach decreasing LDL oxidation with a water extract of *Hibiscus sabdariffa* or treating arteriosclerosis with an extract of *Hibiscus sabdariffa*.

Clarke et al. and Brink: The present invention, as encompassed by cancelled claim 14 and newly amended claim 1, is drawn to method of treating arteriosclerosis by decreasing the oxidation of low density lipoproteins which comprises administering an effective amount of a *Hibiscus sabdariffa* water extract; wherein oxidation of low density lipoproteins is decreased by the *Hibiscus sabdariffa* water extract. However, neither reference discloses administering a *Hibiscus sabdariffa* water extract for treating arteriosclerosis. Clarke et al. teaches an extract of cultured plant cell gum and Brink teaches an extract from guggul.

As such, these references fail to teach or suggest the present invention, which requires the feature of administering a *Hibiscus sabdariffa* water extract and do not anticipate the invention.

Ibnusaud et al. and JP 09295928A: Both of these references pertain to alcohol extracted *Hibiscus* preparations. Claim 1 has been amended to recite the use of a water extract of *Hibiscus*

sabdariffa. This amendment is supported by page 4, third paragraph of the specification. A chemist of ordinary skill in the art would readily recognize that the solvent used for extraction dictates the product obtained. As such, a "water extract" as used in the present invention is a different composition than an "alcohol extract" as used in the prior art. As such, the use of a water extract of *Hibiscus sabdariffa* distinguishes the invention from these references. Applicants further note that the JP '928A reference pertains to topical preparations rather than systemically administered compositions as inherently required with the present invention. Withdrawal of the rejections is therefore respectfully requested.

JP 10366005 and JP2000095663A: Both of JP '005 and JP '663 are directed to topical administration of preparations of *Hibiscus sabdariffa*. As such, neither reference discloses a method of inhibiting LDL oxidation by administering an extract from *Hibiscus sabdariffa*. The present invention inherently requires internal/systemic administration. Thus, a topical preparation would not achieve the invention. As such, the present invention is distinguished from JP '005 and JP '663.

JP 2000239164: JP '164 discloses the administration of a specific glycosidase inhibitor compound. Glycosidases are enzymes that catalyze the attachment of carbohydrate moieties to proteins. Glycosidases have nothing to do with LDL oxidation. As such, JP '164 fails to disclose or anticipate the present invention.

JP56029522A, FR 2454277A and CN 1156552A: Applicant acknowledge that both JP '522A and FR '277A disclose the preparation of a beverage of *Hibiscus sabdariffa*. FR '277A and CN 655A are directed to dietary uses of *Hibiscus sabdariffa* and fail to disclose any medicinal applications.

JP '552A discloses that the beverage may reduce cholesterol. However, the rejection fails from two aspects. First the Examiner makes the erroneous statement regarding the invention that claim 14 (claim 1) only requires the administration of an extract of *Hibiscus sabdariffa*. This statement is incorrect because it ignores the explicitly recited feature of the invention that "oxidation of low density lipoproteins is inhibited by the *Hibiscus sabdariffa* water extract." In addition, with the instant claims, the preamble clearly breathes life and meaning into the claims with the recitation that the invention is a "method of treating arteriosclerosis by decreasing the oxidation of low density lipoproteins." Thus, the mechanism of action of the invention is

clearly recited in both the preamble and the body of the claims. The present invention requires the inhibition of the oxidation of low density lipoproteins and a treatment of arteriosclerosis.

There also appears to be a second erroneous assumption about the invention regarding the relationship between cholesterol levels and atherosclerosis. JP '522 is relied on for teaching that the beverage of the reference reduces cholesterol. However as evidenced by Glass et al. Cell, 104:503-516 (2001), a copy of which is attached, atherosclerosis does not necessarily correlate with an elevated serum cholesterol. As illustrated in Figure 2 of Glass et al., LDL is a specific group of proteins that carries cholesterol in the blood (compared to general "serum cholesterol"). The oxidation of LDL is an initiating event for the development of atherosclerosis regardless of the serum cholesterol level. Glass et al. state, "even among individuals with the same cholesterol levels there is great disparity in the expression of the clinical disease...." It is generally accepted that LDL is a major player in atherosclerosis, with no involvement of the blood cholesterol levels. Thus, there is an entire population of atherosclerosis patients that would respond to inhibition of LDL oxidation, wherein there is no elevated cholesterol. Neither JP '522 nor FR '277A disclose the specific treatment of atherosclerosis by

inhibiting/decreasing the oxidation of LDL. As such, the references fail to teach or anticipate the present invention.

Claims 1, 5-7 and 14 have been rejected under 35 U.S.C. §102(b) as being anticipated by JP '522 or Tamaki et al. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The invention of claim 1 is drawn to a method of treating arteriosclerosis by decreasing oxidation of low density lipoproteins by administering an effective amount of a *Hibiscus sabdariffa* water extract to a patient in need thereof; wherein oxidation of low density lipoproteins is decreased by the *Hibiscus sabdariffa* water extract. As discussed above, JP '522 teaches that an extract of *Hibiscus sabdariffa* may lower cholesterol levels. Tamaki et al. similarly teach that an extract of *Hibiscus sabdariffa* may lower cholesterol levels.

However, the disclosure in JP '522 and Tamaki et al. regarding cholesterol is different from a method of decreasing the oxidation of LDL or treating atherosclerosis by decreasing LDL. As discussed above, the oxidation of LDL is not indicative of serum cholesterol levels. The oxidation of LDL has been shown to be associated with atherosclerosis, while there may be no change in the cholesterol. As such, a teaching of administering an extract to lower

cholesterol does not anticipate, either explicitly or inherently, a method of treating arteriosclerosis by decreasing the oxidation of LDL because the patient population is different.

Rejection under 35 U.S.C. §103

Claims 1, 5-7 and 14 have been rejected under 35 U.S.C. §103 as being obvious over CN 1156552, JP 2000095663, JP 2000239164, JP 09295928, Tamaki et al., JP2000154134, Ibnsaud et al., Clarke et al. or FR 2454277 combined with JP 56029522 and Brink. Claims 1, 5-7 and 14 have been further rejected as being obvious over JP '522 or Tamaki et al. in view of Brink. Applicants traverse these rejections and withdrawal thereof is respectfully requested.

As discussed above, all of the references fail to teach decreasing LDL oxidation or treating arteriosclerosis by administering a water extract of *Hibiscus sabdariffa*. Lowering cholesterol is not synonymous with decreasing LDL oxidation because LDL oxidation often occurs without an elevated cholesterol level. In addition, arteriosclerosis may occur without a corresponding elevation in cholesterol level. As such, the invention is neither achieved nor suggested by the prior art references. Withdrawal of the rejection is therefore respectfully requested.

Applicants request a three (3) month extension of time for filing the present response. The required fee is attached to the concurrently submitted Notice of Appeal.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong (Reg. No. 40,069) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By ma arm
MaryAnne Armstrong, PhD, #40,069

KM/MAA:
4867-0101P

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000